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EXAMINER	
DICKINSON, PAUL W	

ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,125	SHALABY, SHALABY W.	
	Examiner	Art Unit	
	PAUL DICKINSON	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/4/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. None of the somatostatin analogues meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are as their chemical structures are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus of somatostatin analogues encompassed by the claim, since there is no description of the structural relationship of these derivatives provided in the specification and Applicant has not provided a description as to how the base molecule may be changed while remaining a derivative.

The appearance of mere indistinct words (here the word “analog”) in a specification or a claim, even an original claim, does not necessarily satisfy the written description requirement. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886, 1892 (CAFC 2004).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "at least one terminal segment derived from" is indefinite because it is unclear how far one can deviate from the parent compound without the "derivative" being so far removed therefrom as to be a completely different compound. Similarly, the term "somatostatin analog" is indefinite because it is unclear how far one can deviate from the parent compound.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim is 1 rejected under 35 U.S.C. 102(b) as being anticipated by EP 0952171 (EP '171; document provided by Applicant). EP '171 discloses polyester copolymers and their utility in providing a protective barrier to prevent post-surgical adhesion, treatment of defects in conduits such as blood vessels, and controlled release of a biologically active agent for modulating cellular events such as wound healing and tissue regeneration (see abstract; ¶ 22-34). Triblock copolymers comprising a central polyoxyethylene segment and a terminal polyester segment formed from glyclide, lactide, and epsilon-caprolactone (cyclic monomers) are disclosed (see ¶ 53-57). Di-lactide/glycolide is exemplified (see Example I). The end groups can optionally be carboxylated by an acylation with an appropriate agent, such as succinic anhydride (see ¶ 54). The bioactive compounds to be incorporated include non-steroidal anti-inflammatory agents such as naproxen and anti-cancer drugs such as somatostatin analogs (antiangiogenic peptides), and mixtures thereof (see ¶ 57 and 66). The reference discloses that a combination of two or more drugs may be necessary for optimal effectiveness (see ¶ 66). The polymers may have one or more ionically bound bioactive peptides or a proteins, such as naproxen (see ¶ 46, 32, and 84; Example XV).

The phrase "stent coating composition for multifaceted prevention of vascular restensosis through a plurality of physicopharmacological modes" is an intended use. A recitation of an intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In the instant case, the

composition disclosed by EP '171 is fully capable of being used as a stent coating for multifaceted prevention of vascular restensosis through a plurality of physicopharmacological modes.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by WO 9921908 (WO '908; document provided by Applicant). WO '908 discloses biodegradable polymeric implants comprising at least one bioactive compound and a segmented copolymer comprising a central polyoxyethylene segment and at least one terminal segment obtained by the ring opening polymerization of lactide, glycolide, and/or caprolactone (see page 3, line 33 to page 4, line 11; page 8, lines 16-29; Example 1). The compositions can be used for solid implants that provide controlled release of drug for local delivery (page 20, lines 7-20). Bioactive compounds to be incorporated into the polymer include anti-restenosis, anti-angiogenic drugs such as paclitaxel, which are advantageous to prevent narrowing of blood vessels during or after stent implantation (see page 17, line 20; page 22, line 3 to page 23, line 6; page 2, lines 9-25). The reference contemplates injecting the composition into the vascular wall at the same time and location that a stent is implanted (see page 17-25; page 30, line 29 to page 31, line 4). A wide range of bioactive compounds may be incorporated into the polymer, including antiangiogenic, antineoplastic, anti-platelet, and anti-inflammatory drugs (see page 29, line 8 to page 30, line 28; page 34, line 21 to page 35, line 21). Genistein is a non-steroidal anti-inflammatory (see page 35, lines 10-15).

The phrase "stent coating composition for multifaceted prevention of vascular restensosis through a plurality of physicopharmacological modes" is an intended use. The composition disclosed by WO '908 is fully capable of being used as a stent coating for multifaceted prevention of vascular restensosis through a plurality of physicopharmacological modes.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 11-12, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0952171 (EP '171; document provided by Applicant). The relevant portions of EP '171 are described above in the rejection of Claim 1 under 35 U.S.C. 102(b). EP '171 fails to disclose a specific combination of a basic antiangiogenic compound and an acidic non-steroidal anti-inflammatory.

It would be obvious to one of ordinary skill in the art at the time the invention was made to prepare a polymer as disclosed by EP '171 comprising an ionic conjugate of naproxen (an acidic non-steroidal anti-inflammatory) and a somatostatin analog (a basic antiangiogenic peptide), as this is one embodiment taught by EP '171 that provides a polyester copolymer useful as a protective barrier to prevent post-surgical adhesion, treatment of defects in conduits such as blood vessels, and controlled release of a biologically active agent for modulating cellular events such as wound healing and tissue regeneration.

Claims 1, 3-4, and 9-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0952171 (EP '171; document provided by Applicant) in view of US 20020041893 ('893). The relevant portions of EP '171 are described above in the rejection of Claim 1 under 35 U.S.C. 102(b). EP '171 fails to disclose introduction of at

least one carboxyl end group by acylation of a terminal segment with glutaric anhydride (see Instant Claim 3). EP '171 further fails to disclose lanreotide and trapidil ionically conjugated to the polymer.

'893 discloses sustained release ionic conjugates which contain a free carboxyl group containing biodegradable polymer and a free amino group-containing drug which are ionically bound to each other (see abstract). The rate of release in such drug bound polymers can be optimized by adjusting polymer degradation parameters and surface area (see ¶ 4-5). The drug to be bound must have one or more free amine groups (see ¶ 15). In one embodiment the drugs are acid-stable peptides such as are LHRH, somatostatin, and lanreotide (see ¶ 15; Example 1). The biodegradable polymer contains at least one carboxyl group through which the drug is bound (see abstract). The carboxyl group is introduced into polyesters such as poly(lactic acid) and poly(glycolic acid) by acylation with an appropriate agent, such as glutaric anhydride (see ¶ 14).

Both EP ‘171 and ‘893 are drawn to ionic conjugates of polyester polymers and peptides. Thus, it would be obvious to one of ordinary skill in the art at the time the invention was made to combine the references to afford the instant invention. Specifically, it would be obvious to introduce a carboxyl group into the polymer disclosed by EP ‘171 through acylation of the terminal di-lactide/glycolide with glutaric anhydride. The expectation of success is high, as EP '171 contemplates acylation of the terminal di-lactide/glycolide with an appropriate agent. It would be further obvious to bind a combination of drugs to the polymer, such as lanreotide and trapidil, as both of

these compounds meet the structural requirements for such binding (their structures have at least one free amine), and both compounds, lanreotide, a anti-restenosis agent, and trapidil, a vascodilator, are useful drugs to be administered in conjunction with a cardiac stent to prevent reocculsion of the blood vessel, or generally administered to promote wound healing.

Claims 1-4 and 9-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0952171 (EP '171; document provided by Applicant) in view of US 20020041893 ('893) in further view of US 5149747 ('747). The relevant portions of EP '171 are described above in the rejection of Claim 1 under 35 U.S.C. 102(b). EP '171 fails to disclose introduction of at least one carboxyl side group by free-radically achieved maleation.

As stated above, '893 discloses sustained release ionic conjugates which contain a free carboxyl group containing biodegradable polymer and a free amino group-containing drug which are ionically bound to each other (see abstract). The rate of release in such drug bound polymers can be optimized by adjusting polymer degradation parameters and surface area. The drug to be bound must have one or more free amine groups. In one embodiment the drugs are acid-stable peptides such as are LHRH, somatostatin, and lanreotide. The biodegradable polymer contains at least one carboxyl group through which the drug is bound. The carboxyl group is introduced into polyesters such as poly(lactic acid) and poly(glycolic acid) by acylation with an appropriate agent, such as glutaric anhydride.

‘747 discloses that succinic anhydride, glutaric anhydride, and maleic anhydride are excellent acylating reagents for the preparation of esterified graft polymers (see col 4, lines 51-54).

It would be obvious to one of ordinary skill in the art at the time the invention was made to combine the references to afford the instant invention. Specifically, it would be obvious to introduce a carboxyl side group into the polymer disclosed by EP ‘171 through free-radically achieved maleation (i.e. reaction with maleic anhydride). The expectation of success is high, as EP '171 contemplates acylation of the terminal di-lactide/glycolide with an appropriate agent, and succinic anhydride (disclosed by EP '171), glutaric anhydride (disclosed by '893) and maleic anhydride (disclosed by '747) are known in the art as effective agents for carrying out such acylations.

Claims 1, 4-8, and 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 9921908 (WO ‘908; document provided by Applicant). The relevant portions of WO '908 are described above in the rejection of Claim 1 under 35 U.S.C 102(b). WO '908 fails to disclose the specific combinations of an antiangiogenic compound and a non-steroidal anti-inflammatory compound (see Instant Claim 4), an antineoplastic agent and a non-steroidal anti-inflammatory (see Instant Claim 5), an antineoplastic agent and an anti-platelet aggregation drug (see Instant Claim 6), an antiangiogenic agent and an anti-platelet aggregation drug (see Instant Claim 7), paclitaxel and a non-steroidal anti-inflammatory drug (see Instant platelet. WO ‘908 further fails to disclose a stent coated with the polymer composition.

It would be obvious to one of ordinary skill in the art at the time the invention was made to incorporate the above combinations of agents into the composition disclosed by WO '908 as the reference teaches such combinations as embodiments that provide an effective polymeric drug delivery system that can be implanted within a subject. WO '908 discloses adding the composition into the vascular wall at the same time and place a stent is implanted in order to create a barrier between the stent and the wall, thereby reducing restenosis. It would be obvious to try adding the composition directly to a stent before implantation. This would have several advantages, including easier application (the reference teaches administration as a spray), efficient coating coverage between the stent/vascular wall interface, and potentially improved reduction of restenosis.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL DICKINSON whose telephone number is (571)270-3499. The examiner can normally be reached on Mon-Thurs 9:00am-6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

Paul Dickinson
Examiner
AU 1618

June 30, 2008